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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/805,220	03/22/2004	Kazunari Yamaguchi	Q80490	9623

23373 7590 04/22/2008

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EXAMINER	
CHEN, STACY BROWN	
ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
04/22/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/805,220	YAMAGUCHI ET AL.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17,20-22 and 24-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17,20-22 and 24-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/31/08 has been entered. Claims 17, 20-22 and 24-26 are pending and under examination.

Response to Amendment

2. The following rejections are withdrawn:

- The rejection of claims 17, 20-22 and 24-26 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is withdrawn solely in view of Applicant's amendment.
- The rejection of claims 17, 20-22 and 24-26 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of detecting antibodies that bind BDV, does not reasonably provide enablement for detecting an infection with BDV wherein the infection is either an active infection or a past infection, is withdrawn solely in view of Applicant's amendment.

Claims Summary

3. The claims are drawn to a method for determining whether a subject has been infected with Borna Disease Virus (BDV) by detecting IgM and/or IgG antibodies to BDV antigen polypeptides. The method comprises:

(a) providing a support sensitized with a p10 BDV synthetic antigen polypeptide, and a p24 or p40 BDV antigen polypeptide; or, a support sensitized with p10, p24 and p40;

(b) reacting the support with a sample that is suspected of containing anti-BDV antibodies;

(c) detecting both IgM and IgG antibody, thus detecting infection.

Specifically, the polypeptide from the p24 region is SEQ ID NO: 1. The polypeptide from the p40 region is SEQ ID NO: 3. The polypeptide from the p10 region is SEQ ID NO: 8.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 17, 20-22 and 24-26 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Yamaguchi *et al.* (*Ann. Clin. Biochem.* 2001, 38:348-355, "Yamaguchi"), in view of Watanabe *et al.* (*J. Vet. Med. Sci.*, 2000, 62(7):775-778, "Watanabe"), as evidenced by Planz *et al.* (*Journal of Virology*, 1999, 73:6251-6256, "Planz") and further in view of Hatalski *et al.* (*Journal of Virology*, February 1995, 69(2):741-747, "Hatalski"), and Carbone, K.M. (*Clin.*

Micro. Rev., 2001, 14(3):513-527, "Carbone"). The rejection of record is repeated here for convenience.

Yamaguchi discloses a synthetic peptide-based electrochemiluminescence immunoassay (ECLIA) for anti-BDV p40 and p24 IgG antibodies in rat and horse serum. Yamaguchi teaches the synthesis of 13 peptides having hydrophilic BDV p40 and p24 sequences that were fixed into microbeads. Table 1 discloses a p40 peptide that is identical to Applicant's SEQ ID NO: 3 (PKRRLVDDADAMEDQDLY), and a p24 peptide that is identical to Applicant's SEQ ID NO: 1 (QPVDQLLKDLRKNPS). Rabbit anti-BDV p40 or p24 antiserum was detected by ECLIA immunoassay. ECLIA assay involves the use of an electrode and measurement of photons emitted from the secondary antibodies bound to the BDV antibody-antigen complexes (page 350, first column). The ECLIA method is an immune agglutination reaction method (antigen-antibody binding), and is a fine particle counting method (electrode-photon). Yamaguchi is silent on the use of the antigen polypeptide of p10 (SEQ ID NO: 8) and the aspect of testing for both IgM and IgG antibodies.

However, Watanabe discloses a study on the time course for appearance to antibodies to BDV antigens p40, p24, p18 and p10. Watanabe found that anti-p10 antibodies (IgG) were detected in sera of BDV-infected rats as early as anti-p40 and anti-p24 antibodies (abstract). Watanabe's findings are indicated as useful for establishing diagnostic methods for BDV infection and for understanding its pathogenesis and replication (page 777, second column, last paragraph). It would have been obvious to include the detection of p10 in Yamaguchi's method. One would have motivated to detect anti-p10 antibodies, as well as anti-p40 and anti-p24 antibodies for the purpose of increasing the sensitivity of Yamaguchi's method. Watanabe suggests that antibodies to individual viral proteins and BDV-specific antigens are useful for establishing diagnostic methods (page 777, second column, last paragraph). One would have had a reasonable expectation of success given that Watanabe found anti-p10, anti-p24 and anti-p40 antibodies in serum at the same time (abstract).

Neither Yamaguchi nor Watanabe disclose SEQ ID NO: 8. While Watanabe discloses the use of p10, the sequence of p10 is not disclosed in the Watanabe reference. However, the sequence of p10 includes SEQ ID NO: 8, as evidenced by Planz.

Hatalski discloses the detection of neutralizing antibodies to p40, p23 and gp18 in BDV-infected rats (abstract). Hatalski tested for the presence of both IgG and IgM antibodies to recombinant and native BDV proteins using electrochemiluminescence (page 741, second column, section entitled, "SDS-PAGE, Western blot and immunoprecipitation (IP)"). One would have been motivated to modify Yamaguchi's method by testing for the presence of IgM as well as IgG in order to detect infection as early as possible. Carbone discloses that the first serological evidence of virus infection is often IgM antibody. IgG appears as the immune response matures (page 516, first column, second full paragraph entitled, "Anti-BDV antibody detection"). Given that Hatalski demonstrates that IgM is present in response to BDV infection, and Carbone indicates that IgM is often the first serological evidence of BDV infection, one would have had a reasonable expectation of success that testing for the presence of IgM and IgG would have worked in Yamaguchi's method. Therefore, the invention as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

5. Applicant's arguments have been carefully considered but fail to persuade. Applicant's substantive arguments are primarily directed to the following:

- Applicant argues that Yamaguchi teaches that the ECLIA assay for detecting BDV antibodies can only accurately assess BDV infection when combined with more specific tests, including Western Blot (WB) analysis or the binding inhibition assay based on the addition specific BDV peptides. Applicant points to Yamaguchi, page 354, Discussion section.
  - In response to Applicant's argument, the Office has considered the Discussion section of the Yamaguchi reference. Yamaguchi teaches that the ECLIA disclosed in the paper is able to identify accurately antibodies to BDV in experimentally infected rats and horses (page 354, first column, third full paragraph). Thus, Yamaguchi's ECLIA assay is sufficient to determine whether a subject has been infected with BDV. While it is the Office's position that the ECLIA assay will not distinguish between an acute infection and a cleared infection, the ECLIA assay will determine whether or not an individual was ever infected (exposed) to BDV.
  - Yamaguchi's statement regarding the combination of the ECLIA assay with WB, for example, is merely a suggestion as to an improvement. Yamaguchi does not state that the ECLIA assay will not detect whether an individual has been infected with BDV. Yamaguchi does indicate that the test would be even more accurate when combined with WB or another

binding assay. These suggestions are not absolute requirements to determining whether a subject has been infected with BDV. Yamaguchi's assay is not limited to combinations of ECLIA and WB, but may be performed with the ECLIA assay alone. The degree of accuracy is not represented in the instant claims.

- Applicant argues that Watanabe fails to cure the deficiencies of Yamaguchi because Watanabe discloses only WB.
  - In response to Applicant's argument, the Office is aware that Watanabe teaches WB analysis. Watanabe also discloses the use of an immunoassay to detect anti-p10 antibodies (Figure 1). Watanabe is relied upon for its teaching that anti-p10 antibodies (IgG) were detected in sera of BDV-infected rats as early as anti-p40 and anti-p24 antibodies (abstract). Watanabe's findings are indicated as useful for establishing diagnostic methods for BDV infection and for understanding its pathogenesis and replication (page 777, second column, last paragraph). It would have been obvious to include the detection of p10 in Yamaguchi's method. One would have motivated to detect anti-p10 antibodies, as well as anti-p40 and anti-p24 antibodies for the purpose of increasing the sensitivity of Yamaguchi's method. Watanabe suggests that antibodies to individual viral proteins and BDV-specific antigens are useful for establishing diagnostic methods (page 777, second column, last paragraph).

- The test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

Conclusion

6. No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30), alternate Fridays off,. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Stacy B. Chen/ 4-18-2008
Primary Examiner, TC1600